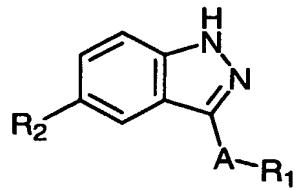


5     What is claimed is:

1.     A method for treating, preventing and/or managing an asbestos-related disease or disorder in a patient, comprising administering to a patient in need thereof an effective amount of a JNK Inhibitor or a pharmaceutically acceptable salt thereof.
2.     A method for treating, preventing and/or managing an asbestos-related disease or disorder in a patient, comprising administering to a patient in need thereof an effective amount of a compound having the following formula:



or a pharmaceutically acceptable salt thereof,

15    wherein:

A is a direct bond, -(CH<sub>2</sub>)<sub>a</sub>-, -(CH<sub>2</sub>)<sub>b</sub>CH=CH(CH<sub>2</sub>)<sub>c</sub>-, or -(CH<sub>2</sub>)<sub>b</sub>C≡C(CH<sub>2</sub>)<sub>c</sub>-;

R<sub>1</sub> is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted with one to four substituents independently selected from R<sub>3</sub>;

R<sub>2</sub> is -R<sub>3</sub>, -R<sub>4</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>R<sub>6</sub>,

20    -(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>(CH<sub>2</sub>)<sub>c</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)NR<sub>6</sub>R<sub>7</sub>,  
-(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>SO<sub>d</sub>R<sub>5</sub> or -(CH<sub>2</sub>)<sub>b</sub>SO<sub>2</sub>NR<sub>5</sub>R<sub>6</sub>;

a is 1, 2, 3, 4, 5 or 6;

b and c are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

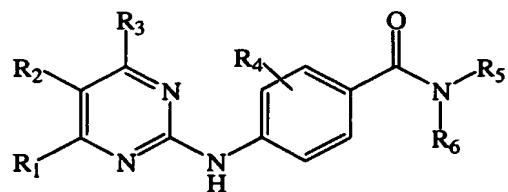
25    d is at each occurrence 0, 1 or 2;

5     $R_3$  is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, heterocycle, heterocycloalkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_2NR_8R_9$ ,  $-NR_8SO_2R_9$ ,  $-CN$ ,  $-NO_2$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

$R_4$  is alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, each being optionally substituted with one to four substituents independently selected from  $R_3$ , or  $R_4$  is halogen or hydroxy;

15     $R_5$ ,  $R_6$  and  $R_7$  are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, wherein each of  $R_5$ ,  $R_6$  and  $R_7$  are optionally substituted with one to four substituents independently selected from  $R_3$ ; and  $R_8$  and  $R_9$  are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocycloalkyl, or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of  $R_8$ ,  $R_9$ , 20 and  $R_8$  and  $R_9$  taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from  $R_3$ .

3.    A method for treating, preventing and/or managing an asbestos-related disease or disorder in a patient, comprising administering to a patient in need thereof an effective amount of a compound having the following formula:



or a pharmaceutically acceptable salt thereof,

30    wherein:

5     $R_1$  is aryl or heteroaryl optionally substituted with one to four substituents independently selected from  $R_7$ ;

$R_2$  is hydrogen;

$R_3$  is hydrogen or lower alkyl;

10     $R_4$  represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

$R_5$  and  $R_6$  are the same or different and independently  $-R_8$ ,  $-(CH_2)_aC(=O)R_9$ ,  $-(CH_2)_aC(=O)OR_9$ ,  $-(CH_2)_aC(=O)NR_9R_{10}$ ,  $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$ ,  $-(CH_2)_aNR_9C(=O)R_{10}$ ,  $(CH_2)_aNR_{11}C(=O)NR_9R_{10}$ ,  $-(CH_2)_aNR_9R_{10}$ ,  $-(CH_2)_aOR_9$ ,  $-(CH_2)_aSO_cR_9$  or  $-(CH_2)_aSO_2NR_9R_{10}$ ;

15    or  $R_5$  and  $R_6$  taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

20     $R_7$  is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

25     $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, aryalkyl, heterocycle or heterocycloalkyl.;

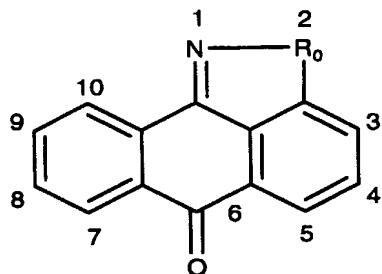
or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are attached to form a heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

5 *c* is at each occurrence 0, 1 or 2.

4. A method for treating, preventing and/or managing an asbestos-related disease or disorder in a patient, comprising administering to a patient in need thereof an effective amount of a compound having the following formula:

10



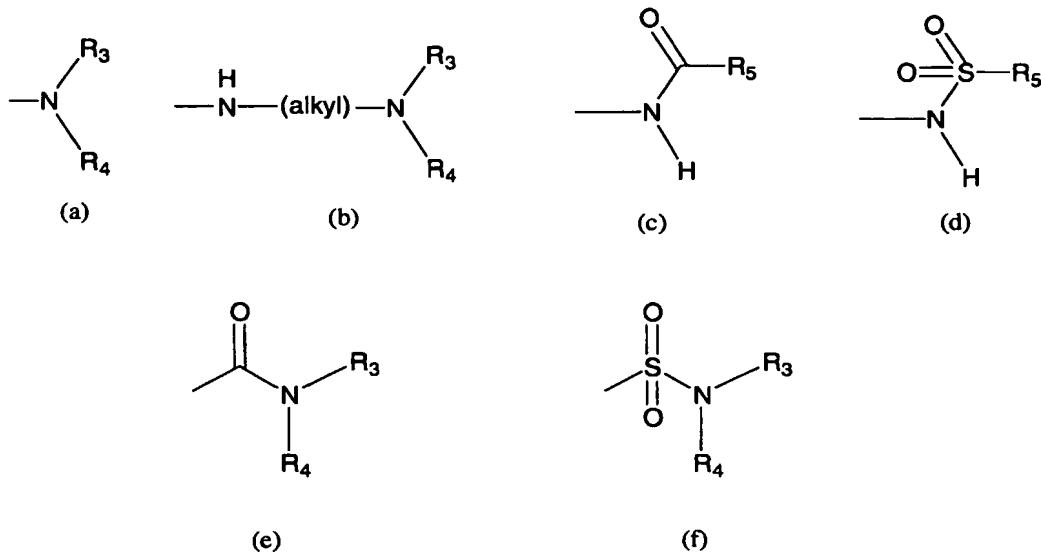
or a pharmaceutically acceptable salt thereof,

wherein R0 is -O-, -S-, -S(O)-, -S(O)2-, NH or -CH2-;

the compound being (i) unsubstituted, (ii) monosubstituted and having a first substituent, or (iii) disubstituted and having a first substituent and a second substituent;

the first or second substituent, when present, is at the 3, 4, 5, 7, 8, 9, or 10 position, wherein the first and second substituent, when present, are independently alkyl, hydroxy, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxy carbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy,

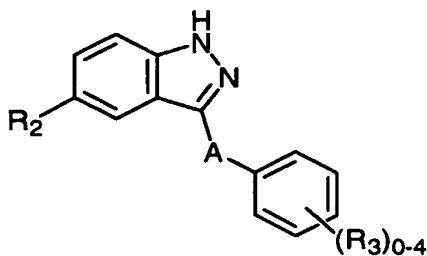
20 aminoalkoxy, mono-alkylaminoalkoxy, di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c), (d), (e), or (f):



5 wherein  $R_3$  and  $R_4$  are taken together and represent alkylidene or a heteroatom-containing cyclic alkylidene or  $R_3$  and  $R_4$  are independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, aminoalkyl, monoalkylaminoalkyl, or di-alkylaminoalkyl; and

10  $R_5$  is hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, alkoxyalkyl, alkoxycarbonylalkyl, amino, mono-alkylamino, di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, cycloalkylalkylamino, aminoalkyl, monoalkylaminoalkyl, or di-alkylaminoalkyl.

5. The method of claim 2 wherein A is a direct bond.
6. The method of claim 2 wherein A is  $-(CH_2)_a-$ .
- 15 7. The method of claim 2 wherein A is  $-(CH_2)_bCH=CH(CH_2)_c-$ .
8. The method of claim 2 wherein A is  $-(CH_2)_bC\equiv C(CH_2)_c-$ .
9. The method of claim 2 wherein the compound has the following formula:



or a pharmaceutically acceptable salt thereof,

wherein:

A is a direct bond, -(CH<sub>2</sub>)<sub>a</sub>-, -(CH<sub>2</sub>)<sub>b</sub>CH=CH(CH<sub>2</sub>)<sub>c</sub>-, or -(CH<sub>2</sub>)<sub>b</sub>C≡C(CH<sub>2</sub>)<sub>c</sub>;

R<sub>1</sub> is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted

10 with one to four substituents independently selected from R<sub>3</sub>;

R<sub>2</sub> is -R<sub>3</sub>, -R<sub>4</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>R<sub>6</sub>, -  
(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>(CH<sub>2</sub>)<sub>c</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)NR<sub>6</sub>R<sub>7</sub>, -  
(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>SO<sub>d</sub>R<sub>5</sub> or -(CH<sub>2</sub>)<sub>b</sub>SO<sub>2</sub>NR<sub>5</sub>R<sub>6</sub>;

a is 1, 2, 3, 4, 5 or 6;

15 b and c are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

d is at each occurrence 0, 1 or 2;

R<sub>3</sub> is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, 20 heterocycle, heterocycloalkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>2</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>2</sub>R<sub>9</sub>, -CN, -NO<sub>2</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>OR<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>R<sub>9</sub>, -O(CH<sub>2</sub>)<sub>b</sub>NR<sub>8</sub>R<sub>9</sub>, or heterocycle fused to phenyl;

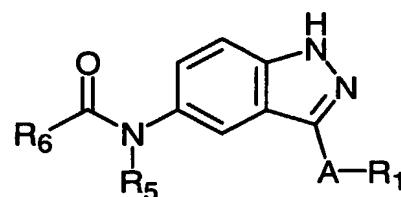
R<sub>4</sub> is alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, each being optionally substituted with one to four substituents independently selected from R<sub>3</sub>, or R<sub>4</sub> is halogen 25 or hydroxy;

5  $R_5$ ,  $R_6$  and  $R_7$  are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, wherein each of  $R_5$ ,  $R_6$  and  $R_7$  are optionally substituted with one to four substituents independently selected from  $R_3$ ; and

10  $R_8$  and  $R_9$  are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocycloalkyl, or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of  $R_8$ ,  $R_9$ , and  $R_8$  and  $R_9$  taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from  $R_3$ .

10. The method of claim 2 wherein the compound has the following formula:

15



or a pharmaceutically acceptable salt thereof,

wherein:

20 A is a direct bond, -(CH<sub>2</sub>)<sub>a</sub>-, -(CH<sub>2</sub>)<sub>b</sub>CH=CH(CH<sub>2</sub>)<sub>c</sub>-, or -(CH<sub>2</sub>)<sub>b</sub>C≡C(CH<sub>2</sub>)<sub>c</sub>-,

$R_1$  is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted with one to four substituents independently selected from  $R_3$ ;

$R_2$  is - $R_3$ , - $R_4$ , -(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>C(=O)NR<sub>5</sub>(CH<sub>2</sub>)<sub>c</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>C(=O)NR<sub>6</sub>R<sub>7</sub>, -

25 (CH<sub>2</sub>)<sub>b</sub>NR<sub>5</sub>R<sub>6</sub>, -(CH<sub>2</sub>)<sub>b</sub>OR<sub>5</sub>, -(CH<sub>2</sub>)<sub>b</sub>SO<sub>d</sub>R<sub>5</sub> or -(CH<sub>2</sub>)<sub>b</sub>SO<sub>2</sub>NR<sub>5</sub>R<sub>6</sub>;

$a$  is 1, 2, 3, 4, 5 or 6;

$b$  and  $c$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

5 *d* is at each occurrence 0, 1 or 2;

*R*<sub>3</sub> is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>2</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>2</sub>R<sub>9</sub>, -CN, -NO<sub>2</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>OR<sub>9</sub>, -

10 NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>R<sub>9</sub>, -O(CH<sub>2</sub>)<sub>b</sub>NR<sub>8</sub>R<sub>9</sub>, or heterocycle fused to phenyl;

*R*<sub>4</sub> is alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, each being optionally substituted with one to four substituents independently selected from *R*<sub>3</sub>, or *R*<sub>4</sub> is halogen or hydroxy;

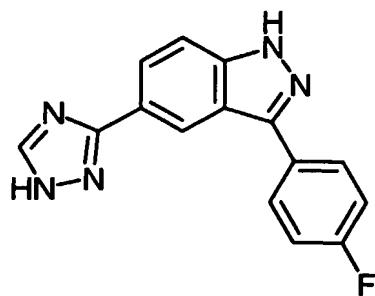
*R*<sub>5</sub>, *R*<sub>6</sub> and *R*<sub>7</sub> are the same or different and at each occurrence independently hydrogen,

15 alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, wherein each of *R*<sub>5</sub>, *R*<sub>6</sub> and *R*<sub>7</sub> are optionally substituted with one to four substituents independently selected from *R*<sub>3</sub>; and

*R*<sub>8</sub> and *R*<sub>9</sub> are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocycloalkyl, or *R*<sub>8</sub> and *R*<sub>9</sub> taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of *R*<sub>8</sub>, *R*<sub>9</sub>,

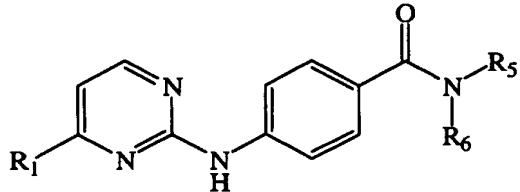
20 and *R*<sub>8</sub> and *R*<sub>9</sub> taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from *R*<sub>3</sub>.

11. The method of claim 2 wherein the compound has the following formula:



25 or a pharmaceutically acceptable salt thereof.

5 12. The method of claim 3, wherein the compound has the following formula:



or a pharmaceutically acceptable salt thereof,

wherein:

10 R<sub>1</sub> is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R<sub>7</sub>;

R<sub>2</sub> is hydrogen;

R<sub>3</sub> is hydrogen or lower alkyl;

15 R<sub>4</sub> represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)R<sub>9</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>, (CH<sub>2</sub>)<sub>a</sub>NR<sub>11</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>OR<sub>9</sub>, -

20 (CH<sub>2</sub>)<sub>a</sub>SO<sub>c</sub>R<sub>9</sub> or -(CH<sub>2</sub>)<sub>a</sub>SO<sub>2</sub>NR<sub>9</sub>R<sub>10</sub>;

or R<sub>5</sub> and R<sub>6</sub> taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R<sub>7</sub> is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl,

25 arylalkyl, heterocycle, heterocycloalkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>c</sub>R<sub>8</sub>, -SO<sub>c</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>c</sub>R<sub>9</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -

5     $\text{NR}_8\text{C}(=\text{O})(\text{CH}_2)_b\text{OR}_9$ ,  $-\text{NR}_8\text{C}(=\text{O})(\text{CH}_2)_b\text{R}_9$ ,  $-\text{O}(\text{CH}_2)_b\text{NR}_8\text{R}_9$ , or heterocycle fused to phenyl;

$\text{R}_8$ ,  $\text{R}_9$ ,  $\text{R}_{10}$  and  $\text{R}_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, heterocycle, heterocycloalkyl;

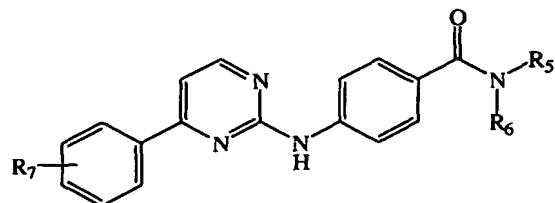
10    or  $\text{R}_8$  and  $\text{R}_9$  taken together with the atom or atoms to which they are attached to form a heterocycle;

$a$  and  $b$  are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

15     $c$  is at each occurrence 0, 1 or 2.

15

13.    The method of claim 3, wherein the compound has the following formula:



20    or a pharmaceutically acceptable salt thereof,

wherein:

$\text{R}_1$  is aryl or heteroaryl optionally substituted with one to four substituents independently selected from  $\text{R}_7$ ;

$\text{R}_2$  is hydrogen;

25     $\text{R}_3$  is hydrogen or lower alkyl;

$\text{R}_4$  represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

5 R<sub>5</sub> and R<sub>6</sub> are the same or different and independently -R<sub>8</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)R<sub>9</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>C(=O)NR<sub>9</sub>(CH<sub>2</sub>)<sub>b</sub>C(=O)R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>NR<sub>9</sub>C(=O)R<sub>10</sub>, (CH<sub>2</sub>)<sub>a</sub>NR<sub>11</sub>C(=O)NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>NR<sub>9</sub>R<sub>10</sub>, -(CH<sub>2</sub>)<sub>a</sub>OR<sub>9</sub>, -(CH<sub>2</sub>)<sub>a</sub>SO<sub>c</sub>R<sub>9</sub> or -(CH<sub>2</sub>)<sub>a</sub>SO<sub>2</sub>NR<sub>9</sub>R<sub>10</sub>;

10 or R<sub>5</sub> and R<sub>6</sub> taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R<sub>7</sub> is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl, -C(=O)OR<sub>8</sub>, -OC(=O)R<sub>8</sub>, -C(=O)NR<sub>8</sub>R<sub>9</sub>, -C(=O)NR<sub>8</sub>OR<sub>9</sub>, -SO<sub>c</sub>R<sub>8</sub>, -SO<sub>c</sub>NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>SO<sub>c</sub>R<sub>9</sub>, -NR<sub>8</sub>R<sub>9</sub>, -NR<sub>8</sub>C(=O)R<sub>9</sub>, -

15 NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>OR<sub>9</sub>, -NR<sub>8</sub>C(=O)(CH<sub>2</sub>)<sub>b</sub>R<sub>9</sub>, -O(CH<sub>2</sub>)<sub>b</sub>NR<sub>8</sub>R<sub>9</sub>, or heterocycle fused to phenyl;

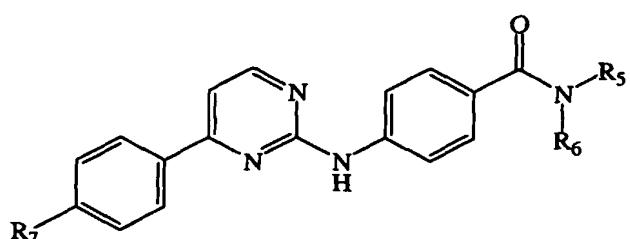
R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl;

or R<sub>8</sub> and R<sub>9</sub> taken together with the atom or atoms to which they are attached to form a heterocycle;

a and b are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

25 14. The method of claim 3, wherein the compound has the following formula:



or a pharmaceutically acceptable salt thereof,

5 wherein:

$R_1$  is aryl or heteroaryl optionally substituted with one to four substituents independently selected from  $R_7$ ;

$R_2$  is hydrogen;

$R_3$  is hydrogen or lower alkyl;

10  $R_4$  represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

$R_5$  and  $R_6$  are the same or different and independently  $-R_8$ ,  $-(CH_2)_aC(=O)R_9$ ,  $-(CH_2)_aC(=O)OR_9$ ,  $-(CH_2)_aC(=O)NR_9R_{10}$ ,  $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$ ,  $-(CH_2)_aNR_9C(=O)R_{10}$ ,  $(CH_2)_aNR_{11}C(=O)NR_9R_{10}$ ,  $-(CH_2)_aNR_9R_{10}$ ,  $-(CH_2)_aOR_9$ ,  $-(CH_2)_aSO_cR_9$  or  $-(CH_2)_aSO_2NR_9R_{10}$ ;

15 or  $R_5$  and  $R_6$  taken together with the nitrogen atom to which they are attached to form a heterocycle;

20  $R_7$  is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl,  $-C(=O)OR_8$ ,  $-OC(=O)R_8$ ,  $-C(=O)NR_8R_9$ ,  $-C(=O)NR_8OR_9$ ,  $-SO_cR_8$ ,  $-SO_cNR_8R_9$ ,  $-NR_8SO_cR_9$ ,  $-NR_8R_9$ ,  $-NR_8C(=O)R_9$ ,  $-NR_8C(=O)(CH_2)_bOR_9$ ,  $-NR_8C(=O)(CH_2)_bR_9$ ,  $-O(CH_2)_bNR_8R_9$ , or heterocycle fused to phenyl;

25  $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl; or  $R_8$  and  $R_9$  taken together with the atom or atoms to which they are attached to form a heterocycle;

5    *a* and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

*c* is at each occurrence 0, 1 or 2.

15.    The method of claim 4, wherein  $R_0$  is -O-.

10

16.    The method of claim 4, wherein  $R_0$  is -S-.

17.    The method of claim 4, wherein  $R_0$  is -S(O)-.

15

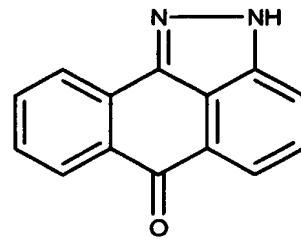
18.    The method of claim 4, wherein  $R_0$  is -S(O)<sub>2</sub>-.

19.    The method of claim 4, wherein  $R_0$  is NH.

20.    The method of claim 4, wherein  $R_0$  is  $CH_2$ -.

20

21.    The method of claim 4, wherein the compound has the following formula:



or a pharmaceutically acceptable salt thereof.

25

22.    The method of claim 1, further comprising administering a second active agent.

23.    The method of claim 2, further comprising administering a second active agent.

24.    The method of claim 3, further comprising administering a second active agent.

5 25. The method of claim 4, further comprising administering a second active agent.

26. The method of claim 22, wherein the second active agent is an anti-cancer agent, antibiotic, anti-inflammatory agent, steroid, immunomodulatory agent, cytokine, immunosuppressive agent, an IMiD®, a SelCID® or a combination thereof.

10 27. The method of claim 23, wherein the second active agent is anthracycline, platinum, alkylating agent, interferon, oblimersen, cisplatin, cyclophosphamide, irinotecan, topotecan, temozolomide, temodar, carboplatin, procarbazine, gliadel, tamoxifen, methotrexate, taxotere, capecitabine, cisplatin, thiotepe, fludarabine, liposomal daunorubicin, cytarabine, doxetaxol, paclitaxel, vinblastine, GM-CSF, IL-2, dacarbazine, vinorelbine, zoledronic acid, palmitronate, biaxin, busulphan, prednisone, 15 bisphosphonate, arsenic trioxide, vincristine, doxorubicin, paclitaxel, ganciclovir, adriamycin, bleomycin, hyaluronidase, mitomycin C, mepacrine, thiotepe, tetracycline, thalidomide or gemcitabine.

20 28. The method of claim 1, wherein the disease or disorder is mesothelioma, asbestosis, pleural effusion, pleural plaque, pleural calcification, diffuse pleural thickening, round atelectasis, or bronchogenic carcinoma.

25 29. A method of treating, preventing or managing an asbestos-related disease or disorder, which comprises administering to a patient in need of such treatment, prevention or management an effective amount of a JNK Inhibitor, or a pharmaceutically acceptable salt thereof, before, during or after chemotherapy, photodynamic therapy, surgery, radiation therapy, gene therapy, or immunotherapy.